REMARKS

Claims 1-28 are pending. Applicants have amended claims 1, 7, 8, 13, 15, 16, 21, 23, and 24. Applicants respectfully request entry and consideration of these amendments in order to facilitate prosecution in this application and to more clearly delineate the claimed subject matter. These amendments are made without waiver or prejudice to future prosecution in later applications claiming priority from this application. Support for these amendments appears throughout the specification and claims as originally filed. No new matter is introduced by these amendments.

Rejection under 35 U.S.C. 112, second paragraph

Claims 1-28 are rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 13, and 27 (and dependent claims thereon) are alleged to be indefinite for reciting "suitable for mycelia attachment". As claims 1, 13, and 27, as amended, no longer recite this language, the rejection is rendered moot.

Claims 7, 15, and 23 (and dependent claims thereon) are alleged to be indefinite because it is considered unclear if step b. additionally comprises culturing said fungi/species prior to introduction into said medium or if step b. is replaced with culturing fungi prior to introduction into said medium. As claims 7, 15, and 23, as amended hereby, now recite that step b. further comprises culturing said fungi/species (as opposed to "is replaced with"), Applicants submit that these claims are no longer indefinite and request withdrawal of this rejection.

Claim 24 is alleged to lack sufficient antecedent basis for the "filamentous fungi" limitation in line 4. Claim 24, as amended hereby, now recites the limitation "*Monascus* species", which is supported and finds antecedent basis in base claim 21, from which claim 24 depends. Applicants request withdrawal of this rejection.

Rejection under 35 U.S.C. 102(b)

Claims 1 - 4, 13, and 21 are rejected as being anticipated by Yamaguchi et al. U.S. Patent No. 3,765,906 ("Yamaguchi"). It is alleged in the Action that: (a) Yamaguchi teaches a culture medium containing rice powder in which a *Monascus* species is inoculated; (b) it is inherent in the methods of Yamaguchi that rice powder substrate was suitable for mycelia attachment because it is a nutritionally solid grain substrate; and (c) by practicing the methods of Yamaguchi, it is inherent that one would be practicing the methods as claimed by Applicant. Applicants disagree.

The allegation is based on an oversimplification of assertion (a) above, and further suffers in that assertions (b) and (c) above are untrue. Yamaguchi teaches a submerged culture medium containing 2% rice powder (e.g., Example 1 in Yamaguchi) used for cultivating a *Monascus* species, however, inherent in such teaching is the fact that the Yamaguchi medium is a homogeneous liquid medium, not a solid substrate medium. Thus, Applicants' solid substrate medium comprising a "suspended nutritionally solid substrate" or "suspended grain substrate", as delineated in independent claims 1, 13, and 21, and discussed throughout the specification as filed, including at page 5, line 26 to page 6, line 2, is distinguishable from Yamaguchi's homogeneous liquid medium. Applicants' nutritionally solid substrate is a substrate which keeps its solid morphology in the medium to provide a place where mycelia can attach to. See, Specification at page 5, lines 26-28. A liquid medium containing rice powder does not contain a substrate which keeps its solid morphology. Thus, assertions (b) and (c) are inaccurate.

Moreover, not only are the physical differences between the liquid (Yamaguchi) and solid (Applicants) mediums evident, but the functional differences in the two mediums are also demonstrated in Example 1 at page 7 of Applicants' specification as filed. The results recited in Applicants' Example 1 show that red pigments produced by using the medium containing suspended rice particles (i.e. solid medium, Applicants) were two-fold greater than those produced by using a rice powder-containing medium (i.e., liquid medium, Yamaguchi). See, Specification at page 8, lines 15-17.

Based on the foregoing remarks, Applicants submit that Applicant's claimed subject matter is distinguishable from (both physically and functionally), and not anticipated by, Yamaguchi. Applicants request withdrawal of this rejection.

Rejection under 35 U.S.C. 103(a)

Claims 6, 11-12, 19-20, and 27-28 are rejected as being unpatentable over Yamaguchi et al. U.S. Patent No. 3,765,906 ("Yamaguchi") in view of Johal et al. U.S. Patent No. 4,954,440 ("Johal") and Eyal et al. U.S. Patent No. 5,077,201 ("Eyal"). In the Action, it is alleged that Yamaguchi teaches a nutritionally solid substrate that is provided in a culture medium in which a *Monascus* species is inoculated, then it is alleged that Johal provides motivation for adding other materials (e.g., nitrogen source, nutrients, etc.) as well as the use of batch fermentation and the fed batch process, and finally it is alleged that Eyal further supports the motivation to employ the fed batch process. Applicants disagree.

As delineated above in response to the rejection under 35 U.S.C. 102(b), the allegation of the teaching of Yamaguchi is an oversimplification and inaccurate, which inaccuracy forms the underlying basis of this rejection. The teaching of Yamaguchi relates to a homogeneous liquid medium, not a solid substrate medium. Applicants' nutritionally solid substrate is a substrate that keeps its solid morphology in the medium to provide a place where mycelia can attach. A homogeneous liquid medium containing rice powder does not contain a substrate that keeps its solid morphology. Yamaguchi provides no motivation in regard to "nutritionally solid substrates" and certainly provides no indication of the greatly improved yield (i.e., two-fold increase in pigment production) that results from the use of nutritionally solid substrates. It is Applicants who first disclose the advantage of utilizing nutritionally solid substrates (see, Specification Example 1) to provide this advantageous and surprising activity. Moreover, neither Johal nor Eyal discuss use of a "suspended nutritionally solid substrate" and certainly provide no indication of the greatly improved yield (i.e., two-fold increase in pigment production) that results from the use of nutritionally solid substrates. In fact, Johal relates to supports that are "fixed" and "chemically and/or biologically inert" (see, Johal at column 3, lines 58-61), clearly teaching away from Applicants' suspended nutritionally solid substrates, which are not inert. **As such, Applicants submit that Yamaguchi, in view of Johal and Eyal, does not render Applicants' subject matter obvious, and request that this rejection be withdrawn.**

Claims 5, 7-8, 14-16, and 22-24 are rejected as being unpatentable over Yamaguchi in view of Yueh et al. U.S. Patent No. 4,418,080 ("Yueh") and Haas et al. U.S. Patent No. 4,031,250 ("Haas"). In the Action, it is alleged that Yamaguchi teaches a nutritionally solid substrate that is provided in a culture medium in which a *Monascus* species is inoculated, then it is alleged that Yueh provides motivation for obtaining an inoculum from a stock culture, and finally it is alleged that Haas provides motivation for a stock culture grown on an agar slant. Applicants disagree.

As delineated above in response to the rejection under 35 U.S.C. 102(b), the allegation of the teaching of Yamaguchi is an oversimplification and inaccurate, which inaccuracy forms the underlying basis of this rejection. The teaching of Yamaguchi relates to a homogeneous liquid medium, not a solid substrate medium. Applicants' nutritionally solid substrate is a substrate that keeps its solid morphology in the medium to provide a place where mycelia can attach. A homogeneous liquid medium containing rice powder does not contain a substrate that keeps its solid morphology. Yamaguchi provides no motivation in regard to "nutritionally solid substrates" and certainly provides no indication of the greatly improved yield that results from the use of nutritionally solid substrates. It is Applicants who first disclose the advantage of utilizing nutritionally solid substrates (see, Specification Example 1) to provide this advantageous and surprising activity. Neither Yueh nor Haas discuss nor intimate the type of improvement disclosed by Applicants. **As such, Applicants submit that Yamaguchi, in view of Yueh and Haas, does not render Applicants' subject matter obvious, and request that this rejection be withdrawn.**

Claims 9-10, 17-18, and 25-26 are rejected as being unpatentable over Yamaguchi in view of Yueh, Haas, and further in view of Tung et al. Bioprocess. Eng. 17(1) pp.1-5 (1997) ("Tung"). In the Action, the same allegations regarding Yamaguchi in view of Yueh and Haas (above) are reiterated, and then it is further alleged that while the above references do not teach the use of a pneumatic airlift bioreactor with a net draft tube, use of such a bioreactor would have been obvious in light of Tung. Applicants disagree.

For the reasons stated above, Applicants submit that Yamaguchi in view of Yueh and Haas do not render claims 9-10, 17-18, and 25-26 obvious. For that reason alone, the rejection further based in view of Tung should also fail. Tung, however, provides no teaching that use of

their bioreactor is useful for *Monascus* species (Tung teaches *Saccharomyces* cerevisiae) nor is any indication made as to what specific processes are particularly amenable for use in their bioreactor. In fact, it is stated in Tung that "[e]xtension of the proposed reactor to other aerobic fermentation processes is possible" (underline added for emphasis) and that "[t]he performance of the airlift reactor with multiple (more than two) concentric net draft tubes requires further investigations." See, Tung at page 4 (last paragraph). Not only does Tung lack a teaching of Applicants' methods as appropriate conditions suitable for their bioreactor, it appears that Tung generally is unclear as to what processes are viable in their bioreactor. Moreover, Tung provides no teaching of Applicants' "suspended nutritionally solid substrate" methods and the surprising greatly improved yields (i.e., two-fold increase in pigment production) produced thereby. **As such, Applicants submit that Yamaguchi, in view of Yueh, Haas, and Tung does not render Applicants' subject matter obvious, and request that this rejection be withdrawn.**

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a $55 check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket number 08415-003001.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 1, 7, 8, 13, 15, 16, 21, 23, and 24 have been amended as follows:

1. (Twice Amended) A method for cultivation of filamentous fungi comprising the steps of:

(a) preparing a medium comprising a suspended nutritionally solid substrate [suitable for mycelia attachment]; and

(b) inoculating said medium with said filamentous fungi in a bioreactor to carry out fermentation wherein the mycelia of said filamentous fungi are attached to said suspended solid substrate.

7. (Twice Amended) The method as claimed in claim 1, wherein step (b) further comprises culturing said filamentous fungi prior to introduction into said medium.

8. (Twice Amended) The method as claimed in claim 7, wherein [step (b)]the culturing comprises:

(1) inoculating said filamentous fungi from a stock culture to a new agar plate and incubating in an incubator for about 5 to 7 days;

(2) washing spores and mycelia of the filamentous fungi grown on said plate with sterile water; and

(3) cultivating for about 36 to 48 hours said spores and mycelia in a medium comprising a nutritionally solid substrate by shaking, to form a culture[; and

(4) inoculating the culture, after being cultivated for about 36 to 48 hours, into the bioreactor].

13. (Twice Amended) A method for cultivation of *Monascus* species by using a suspended grain substrate comprising the steps of:

(a) preparing a medium comprising a suspended grain substrate [suitable for mycelia attachment]; and

(b) inoculating said medium with said *Monascus* species in a bioreactor to carry out fermentation wherein the mycelia of said *Monascus* species are attached to said suspended grain substrate.

15. (Twice Amended) The method as claimed in claim 13, wherein step (b) further comprises culturing said *Monascus* species prior to introduction into said medium.

16. (Twice Amended) The method as claimed in claim 15, wherein [step (b)]the culturing comprises:

(1) inoculating said *Monascus* species from a stock culture to a new agar plate and incubating in an incubator for about 5 to 7 days;

(2) washing spores and mycelia of [the filamentous fungi]said *Monascus* species grown on said plate with sterile water; and

(3) cultivating for about 36 to 48 hours said spores and mycelia in a medium comprising a grain substrate by shaking, to form a culture[; and

(4) inoculating the culture, after being cultivated for about 36 to 48 hours, into the bioreactor].

21. (Twice Amended) A method for producing metabolites from the cultivation of *Monascus* species by using a suspended grain substrate comprising the steps of:

(a) preparing a medium comprising a suspended grain substrate [suitable for mycelia attachment]; and

(b) inoculating said medium with said *Monascus* species in a bioreactor to carry out fermentation wherein the mycelia of said *Monascus* species are attached to said suspended substrate.

23. (Twice Amended) The method as claimed in claim 21, wherein step (b) further comprises culturing said *Monascus* species prior to introduction into said medium.

24. (Twice Amended) The method as claimed in claim 23, wherein [step (b)]the culturing comprises:

(1) inoculating said *Monascus* species from a stock culture to a new agar plate and incubating in an incubator for about 5 to 7 days;

(2) washing spores and mycelia of [the filamentous fungi]said *Monascus* species grown on said plate with sterile water; and

(3) cultivating for about 36 to 48 hours said spores and mycelia in a medium comprising a grain substrate by shaking, to form a culture[; and

(4) inoculating the culture, after being cultivated for about 36 to 48 hours, into the bioreactor].